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10/518,503	12/20/2004	Hans-Michael Eggenweiler	MERCK-2957	7857
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MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			JAISLE, CECILIA M	
			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,503	EGGENWEILER ET AL.	
	Examiner	Art Unit	
	Cecilia M. Jaisle.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 11 October 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-19, 21, 24-26 and 30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) 1-19 is/are allowed.
- 6) Claim(s) 21, 24-26 and 30 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED OFFICE ACTION

Status of Rejections in Office Action of Jul. 11, 2007

Claim 29 was rejected under 35 USC 112, second paragraph as indefinite and incomplete in not defining a completed article of manufacture. This rejection of claim 29 is moot in view of the cancellation thereof.

Claims 1-29 were rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim subject matter that applicant regards as the invention. This rejection of claims 20, 22, 23, and 27-29 is moot in view of the cancellation thereof. This rejection as applied to claims 1-19, 21, 24-26 and 30 is overcome in view of Applicants' amendments to the claims.

Claims 1-29 were rejected under 35 USC 112, first paragraph, because the specification does not reasonably provide enablement for making pharmaceutically usable derivatives of the Formula I compounds embraced thereby. This rejection of claims 20, 22, 23, and 27-29 is moot in view of the cancellation thereof. This rejection as applied to claims 1-19, 21, 24-26 and 30 is overcome in view of Applicants' amendments to the claims.

Claims 20-26 were rejected under 35 USC 112, first paragraph, as failing to comply with the enablement requirement, because the specification does not reasonably enable treatment of all pathological conditions/diseases susceptible to PDE-4 inhibition amelioration with Formula I compounds. This rejection of claims 20, 22 and

23 is moot in view of the cancellation thereof. The rejection is repeated for claims 21, 24-26 and 30 as set forth below.

Rejection Under 35 USC 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 24-26 and 30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibition of proliferation of T-cells (Example I) and control of cytokine production in human peripheral blood monocytes (PBMCs) (Example II), does not reasonably provide enablement for treatment of allergic diseases, asthma, chronic bronchitis, atopic dermatitis, psoriasis or other skin diseases, inflammatory diseases, autoimmune diseases, sepsis, memory disorders, atherosclerosis, AIDS or myocardial disease (claims 21, 24, 25 and 30), coronary heart disease, reversible or irreversible myocardial ischaemia/reperfusion damage, acute or chronic heart failure or restenosis including in-stent restenosis and stent-in-stent restenosis (claim 26) and allergic diseases, asthma, chronic bronchitis, atopic dermatitis, psoriasis, rheumatoid arthritis, multiple sclerosis, Crohn's disease, diabetes mellitus, ulcerative colitis, osteoporosis, transplant rejection reactions, cachexia or atherosclerosis (claim 30). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The present specification offers no evidence

Art Unit: 1624

that the claimed compounds control specific diseases/conditions susceptible to PDE-4 inhibition amelioration, although the claims encompass such diseases/conditions. The following reasons apply to this enablement rejection.

Pursuant to *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue;" see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims.

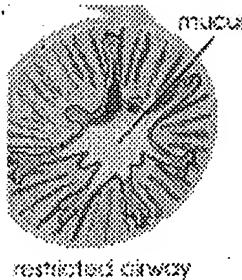
(a) Scope of the compounds.

The scope of the compounds is the trillions of thiazole compounds comprehended under formula I.

(b) Scope of the diseases covered.

The scope of diseases covered has been detailed above. A representative number of these diseases are discussed here to emphasize the scope of such conditions and illnesses.

Asthma is a disease of the lungs that affects bronchial tubes or airways; a reversible obstructive airway disease. Unlike other conditions that obstruct airways,



such as cystic fibrosis, chronic bronchitis and emphysema, asthma does not affect sufferers all of the time. During an asthma attack, membranes inside bronchial tubes release mucus and become inflamed, causing muscles to contract and create wheezing spasms. Attacks can be severe or relatively mild, but the condition is dangerous and can easily spiral out of control. Specific causes of asthma are far from straightforward. Asthma is divided into a number of different types:

- **Allergic Asthma:** Triggered by allergens, e.g., pet dander, pollen, dust mites, pollutants, wood dust, smoke, irritants, chemicals, viral infections, bacteria, stress, emotion, exercise.
- **Childhood Allergic Asthma:** Maternal smoking can contribute to asthma or other infant lung function impairment, even before a child is born. Continued exposure to cigarette smoking can irritate the respiratory tract, making infants and children particularly vulnerable to allergic asthma.
- **Intrinsic Asthma:** Allergies do not play a part; its typical onset occurs after age 40. Possible causes include respiratory irritants, e.g., perfumes, cleaning agents, fumes, smoke, cold air, upper respiratory infections, gastroesophageal reflux. Intrinsic asthma tends to be less responsive to treatment than allergic asthma.
- **Exercise-Induced Asthma:** Can affect anyone at any age and may be attributed to loss of heat and moisture in the lungs with strenuous exercise. Frequent coughing during exercise may be the only symptom, but exercise-induced asthma symptoms

can be more severe in cold, dry conditions. Prophylactic medications can prevent onset of asthmatic symptoms for sensitive individuals.

- **Nocturnal Asthma:** Affects people during sleep, regardless of time of sleep.
 - . Symptoms can be triggered by allergens in bedding or the bedroom, decrease in room temperature, and gastroesophageal reflux.
- **Occupational Asthma:** Occurs as a result of breathing chemical fumes, wood dust, or other irritants over long periods of time.

Steroid-Resistant Asthma: Overuse of asthma medications can lead to status asthmaticus, a severe asthma attack that fails to respond to medication and may require mechanical ventilation.

Ulcerative colitis and Crohn's disease are forms of an entire disorder family known under the generic term, IBD. IBD arises from a range of causes, known and unknown. Ulcerative colitis and Crohn's disease are idiopathic.

Memory disorders comprise all impairment of understanding or skill disorders. These include acquired language disorders, such as aphasias (e.g., conduction aphasia), apraxia, dysarthria, alexia, receptive dysphasia, and agraphia. It includes many types disorders called amnesias. There is anterograde amnesia (new events are not transferred to long-term memory) and retrograde amnesia (inability to recall events that occurred before the onset of amnesia). There is lacunar amnesia (loss of memory about one specific event), Fugue amnesia (Psychogenic amnesia or hysterical amnesia, including "repressed memories"), Childhood amnesia (inability to remember events from early childhood), Transient Global Amnesia (total memory loss), those arising from

Art Unit: 1624

complex partial seizures, and alcoholic blackouts. It also includes various agnosias, such as Prosopagnosia, Integrative agnosias, asognatoagnosia, Associative agnosias, Time Agnosia, Apperceptive agnosia, object agnosia, finger agnosia, phonagnosia, central achromatopsia, topographical agnosia, dyslexia, dyscalculia, right-left disorientation, Optic ataxia and Ocular apraxia, Color Agnosia, Simultanagnosia, Anosognosia, Auditory Agnosia (including amusia and word meaning deafness), and Somatosensory Agnosia (including Microsomatagnosia, Macrosomatagnosia, tactile agnosias and astereoagnosia), constructional dyspraxia, and more general processing disorders such as Cerebral Visual Impairment.

The claims also embrace dozens of immune disorders.

The claimed scope includes treating various disorders/diseases, which are inadequately enabled, based on inhibition of PDE-4. The compounds of Formula (I) are disclosed to inhibit PDE-4 and the specification recites that these compounds are therefore useful to treat all the diseases noted above for which Applicants provide no competent evidence. Further, Applicants have not provided competent evidence that the instantly disclosed tests (pages 21-28, *inter alia*) are highly predictive for all methods of use disclosed and embraced by the claim language for the intended host.

(2) The nature of the invention and predictability in the art:

The invention is directed toward medicine and is physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance:

The direction and guidance provided is very limited. The dosage range information (page 83+, *inter alia*) is vague and meager. Even the broadest range is 25 fold. Moreover, this dosage information is generic, the same for the many disorders covered by the specification. There is no specific direction or guidance regarding a therapeutic regimen or dosage effective specifically for various compounds described for various medical conditions comprehended.

(4) State of the Prior Art:

These compounds are tetrahydropyridazine and dihydropyridazone derivatives with a particular 2-position substitution pattern. So far as this record shows, no such tetrahydropyridazines and dihydropyridazones of any kind have been determined to have PDE-4 inhibition activity, nor to be useful for the treatment of the various diseases construed by the claims.

The comments of Dyke (already of record) on PDE-4 inhibitor efficacy in memory disorders are prophetic. Regarding MS, Dyke suggests, with no clinical data available, that PDE4 inhibitors may be useful as anti-inflammatory agents, but not as disease modifying agents (pg. 1313). Dyke's expert opinion was that, although PDE-4 inhibitors may show promise in the respiratory area, "clinical data in most [other] therapeutic areas with compounds of this class is inconclusive" (pg. 1314). Dyke acknowledges various PDE isoenzymes, but teaches that PDE-4 inhibitors have only been implicated for anti-inflammatory conditions (pg. 1302).

Art Unit: 1624

Hanifin (already of record) reported testing CP80633, CP102995 and CP76593, PDE-4 inhibitors, on atopic dermatitis. Although Hanifin demonstrated clinical efficacy, later researchers, e.g., Griffiths (already of record) noted that CP80633 was "the only PDE-4 inhibitor known to be clinically effective in atopic dermatitis" (page 300). Thus, Hanifin and Griffiths support that not all PDE-4 inhibitors, such as the claimed compounds, are effective against atopic dermatitis.

PDE-4 predominates in inflammatory cells and, specifically, modulates leucocyte activation. PDE-4 inhibitors would be expected to produce bronchodilation and have a certain anti-inflammatory effect, in particular, blocking mediator synthesis (and release) in mast cells and basophiles.

The concept that PDE-4 inhibitors could treat such pathological conditions/diseases generally is contrary to what is known about PDE-4 inhibitors. Some PDE4 inhibitors cause vasculitis (blood vessel inflammation), which has hindered PDE-4 inhibitor clinical investigation. Development of SCH-351591 halted because of acute and chronic vasculitis in small to medium sized arteries, and vasculitis was a significant problem with CI-1018 and Ariflo® (cilmilast). The PDE-4 inhibitor IC542 triggered a generalized inflammatory response with extensive neutrophil infiltration in the gastrointestinal tract, nearby mesentery and thymus.

(5) Working Examples:

Examples 1-7 show production of a meager number of compounds from among the trillions covered by formula I. No *in vivo* biological data of any kind is presented. The working examples do not show formation of any derivatives of compounds of

Art Unit: 1624

formula I. *In vitro* testing is shown only for inhibition of proliferation of T-cells (Example I) and control of cytokine production in human PBMCs (Example II). As stated in *Morton Intrntl. Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190, 1194 (Fed.Cir. 1993):

The specification purports to teach, with over fifty examples, the preparation of the claimed compounds ... However ... there is no evidence that such compounds exist ... [T]he examples ... do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

(6) Skill of those in the art:

The history of the effectiveness of PDE-4 inhibitors is very short. PDE-4 inhibitors have been investigated for disorders including AD, COPD, depression, schizophrenia and chronic lymphocytic leukemia. Except for asthma, such efforts have met with little success. The skill level in the area of PDE-4 therapeutics must therefore be considered to be low. At the time of filing and up to now, FDA has not approved any PDE-4 inhibitor for any disorder treatment. Extensive effort to get cilomilast and Daxas® (roflumilast) to be effective against COPD has been without success, evidence of the skill level in this art. The specification does not describe whether these claimed compounds affect the same isoenzymes as cilomilast and roflumilast.

Many if not most diseases said to be treatable by PDE-4 inhibition, e.g., multiple sclerosis, graft rejection, gastrointestinal disorders, such as ulcerative colitis and Crohn's disease, septic shock, contact dermatitis, dementia, etc., are hard to treat. At present no known drug successfully reverses the course of many of these diseases, including MS, etc., despite many drugs said to inhibit PDE-4.

The state of the art indicates the requirement for undue experimentation.

MacKenzie (already of record) indicates that, although the new generation of PDE-4 inhibitors "display[s] greatly reduced side-effects, ... further study of the potential ancillary involvement of adrenaline and/or glucocorticoids in the enhancement of PDE-4, shown in blood mononuclear white cells of [atopic dermatitis] patients is warranted." The ability of a PDE-4 inhibitor to ameliorate all diseases/conditions of the present claims remains open to further study and proof.

(7) The quantity of experimentation needed:

Substantiation of method of use and its scope is required when the method of use is "speculative," "sufficiently unusual" or not provided. See *Ex parte Jovanovics, et al.*, 211 USPQ 907, 909 (BPAI 1981). Also, note *Hoffman v. Klaus*, 9 USPQ2d 1657 (BPAI 1988) and *Ex parte Powers*, 220 USPQ 924 (BPAI 1982) regarding testing types needed to support *in vivo* methods of use. See also MPEP 2163, et. seq. The application disclosure is insufficient to enable instantly claimed methods based solely on disclosure of inhibition of proliferation of T-cells (Example I) and control of cytokine production in human PBMCs (Example II) by Formula (I) compounds. Such experimentation is potentially open-ended.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Response to Remarks of 10-11-2007 Amendment

Applicants assert that the compounds of Formula I inhibit PDE4 and thus are effective to treat all of the diseases recited by the claims. However, the specification in Examples I and II, at pages 93-94, establishes that compounds of Formula I were only demonstrated to inhibit proliferation of T-cells (Example I) and to control cytokine production in human PBMCs. These are the only methods of use supported by this disclosure and any claims to methods of using the present compounds of Formula I must be limited thereto.

Applicants cite *Ex parte Janin*, 209 USPQ 761 (BPAI 1979), for the premise that an unsupported suggestion that reactants within a class defined by the claims, that are inoperable for a method of use, cannot be the basis for claim rejection. However, that is not the basis of the rejection here. Present Examples I and II are admitted to establish that all Formula I compounds inhibit proliferation of T-cells and control cytokine production in human PBMCs. The specification does not disclose more than that for the Formula I compounds.

Applicants cite *In re Marzocchi*, 169 USPQ 367 (CCPA 1971) for the premise that reasons or evidence must be advanced to challenge Applicants' assertion that all compounds encompassed by the claims are operative for the claimed method. Applicants' assertion of method of use by claims 21, 24-26 and 30 is supposedly based on the presence of PDE4 inhibitory action in the Formula I compounds. The references previously of record to Dyke, Hanifin, Griffiths and MacKenzie, for the reasons

Art Unit: 1624

discussed above, well establish that the ability of a PDE-4 inhibitor to ameliorate all diseases/conditions of the present claims remains open to further study and proof.

Also, the following articles further call into question the ability of all compounds that inhibit PDE4 activity to treat all of the present claimed illnesses conclusively.

Regarding allergies and inflammatory diseases, Bernes, J. Allergy Clin. Immunol., Jul. 2000, pgs. 5-16, report, "most of the PDE4 inhibitors so far tested clinically have had unacceptable side effects, particularly nausea and vomiting. ... subtype-selective inhibitors (of PDE4 isoforms) may be developed that may preserve the anti-inflammatory effect, which having less likelihood of side effects." Neither the present claims nor the present specification acknowledges that any of the compounds of Formula I show effectiveness for specific isoforms of PDE4.

Kobayashi, et al., Mediators of Inflammation, Vol. 2007, Article ID 58901, 9 pgs., merely "suggest that PDE4 inhibitors may be therapeutic agents for various diseases such as asthma ... and rheumatoid arthritis." Regarding coronary disease, Reffelmann, et al., Circulation 2003;108;239-244, note, "In the human pulmonary circulation, the [PDE] isoforms 1, 3, 4 and 5 seem to be involved in regulating pulmonary resistance," but suggests a promising future only for PDE5 and not the other isoforms.

Regarding restenosis and atherosclerosis, Rybalkin, et al., Circ. Res. 2002;90:151-157, report disappointing results, "Because PDE3 and PDE4 isozymes are present in the normal arterial wall as well as in many other tissues, inhibition of these PDEs is likely to cause side-effects, such as vasodilation, nausea, and cardiac arrest." They see a promising future for only one isozyme, PDE1C, "Future studies will reveal if

PDE1C can indeed be targeted to inhibit human SMC [smooth muscle cell] proliferation in restenosis after angioplasty, in-stent restenosis, or in lesions of atherosclerosis."

Lehnart, et al., Cell, Vol. 123, 25-35, Oct. 7, 2005, cautions, "These data suggest that reduced PDE4D activity causes defective RyR2-channel [ryanodine receptor] function associated with heart failure and arrhythmias."

Thus, the state of the prior art well establishes reasons and evidence to doubt the assertion of method of use in the specification.

Applicants' statement that the claims are to be interpreted in light of the level of understanding of one of ordinary skill in the art is acknowledged as true and supports the basis for the present rejection. The prior art medical articles summarized above establish that one of ordinary skill in this art recognizes that the presence of PDE4 inhibitory activity in a compound does not, in and of itself, establish that that compound will treat all of the illnesses recited in the rejected claims. The methods of use of PDE4 inhibitors to treat various indications of the claims is not well established and is not well understood by those of skill in the art. This has been established on an indication (or illness) by indication basis by the discussion of the state of the prior art.

Citing *In re Borkowski, et al.*, 164 USPQ 642 (CCPA 1970), Applicants take the position that working examples are not required to provide enablement. The court in Borkowski recognized, 164 USPQ at 645, "a specification need not contain a working example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation." This specification does contain working Examples I and II and they have been indicated to

Art Unit: 1624

be sufficient to enable method claims to the use of the compounds of Formula I limited thereto. However, since the state of the prior art well establishes that one skilled in the art would not be able to practice the invention of claims 21, 24-26 and 30 without an undue amount of experimentation, this rejection is proper and sustainable.

Allowable Claims

Claims 1-19 are seen to be directed to allowable subject matter. The amendments to these claims presented in the Amendment of Oct. 11, 2007 overcome the rejections of these claims under 35 USC 112, first and second paragraphs, as set forth in the Office Action of Jul. 11, 2007. Claims 1-19 are drawn to thiazole-substituted pyridazines derivatives, a process for their preparation and pharmaceutical compositions thereof. Rochas, US 5859008 and US 6479494, both cited by Applicants, describe arylalkanoyl-pyridazines as PDE-4 inhibitors, however, the presently claimed compounds unobviously have substituted thiazole moieties in place of the aryl moiety of the Rochas patents. In addition, the process for preparation and the pharmaceutical compositions of the present claims describe specific limitations that are not taught or fairly suggested by the Rochas patents.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

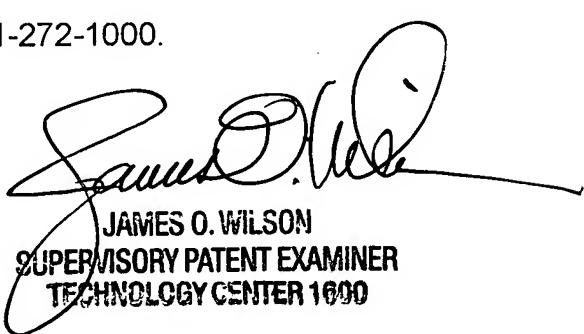
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cecilia M. Jaisle, J.D. whose telephone number is 571-272-9931. The examiner can normally be reached on Monday through Friday; 8:30 am through 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cecilia M. Jaisle, J.D.
11/13/2007



JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600